REMARKS

Claims 11-23, 25-27, 29 and 31-33 are pending in the application. Claim 11 has been amended and claims 28 and 30 have been withdrawn from consideration. The amendments to claim 11 are fully supported by the specification.

In the January 12, 2006 Office Action, claims 11-23, 25-27, 29 and 31-33 were rejected under 35 U.S.C. 112, second paragraph as being indefinite. Claims 11-19, 25-27, 39 and 31-32 were rejected under 35 U.S.C. 102 as anticipated by Agrawal, Crooke, Tuschl, and McSwiggen. The specific grounds for rejection, and applicants' response thereto, are set forth in detail below.

Support for amendment

Support for the amendment to claim 11 is found in the specification at, *e.g.*, page 23, lines 18-24; Figures 11C, 12A, and 15B; and original claim 12.

Rejection Under 35 U.S.C. §112, second paragraph

Claims 11-23, 25-27, 29 and 31-33 are rejected under 35 U.S.C. 112, second paragraph as indefinite. Specifically, the Examiner asserts that it is unclear which nucleotides have a modification at the 2' position. Applicants respectfully traverse because it is clear from the context of the claim and the specification that each of the the nucleotides within the groups of modified nucleotides are modified.

Nevertheless, merely to make explicit that which was implicit, claim 11 has been amended to specify that each nucleotide within a group of modified nucleotides is modified at the 2'-position, thereby obviating the rejection. Claims 12-23, 25-27, 29 and 31-33 depend from claim 11 and therefore, by definition, also contain the same explicit recitation with respect to the modified nucleotides. Accordingly, these dependent claims also fully comply with § 112, second paragraph. Withdrawal of the rejection respectfully is requested.

Rejections Under 35 U.S.C. §102

Claims 11-19, 25-27, 39 and 31-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal, Crooke, Tuschl, and McSwiggen. Applicants respectfully traverse.

In making these rejections, the Examiner asserted that the specification lacks an explicit definition of the term "pattern" and therefore relied upon one of the several alternative definitions of that term as set forth in the Merriam Webster Dictionary, 5th Edition, 1997. (See Office Action at page 3.) The Examiner did not explain why this definition was chosen from the other alternative dictionary definitions, or why the clear meaning of the term "pattern" as used in the specification was not taken into account.

The Federal Circuit has expressly stated that a specification need not provide an explicit definition of a term and that the clear meaning of a claim term may be discerned by implication from the specification. The court further ruled that the specification, and not a dictionary, is the best guide to the meaning of claim terms:

> Assigning such a limited role to the specification, and in particular requiring that any definition of claim language in the specification be express, is inconsistent with our rulings that the specification is "the single best guide to the meaning of a disputed term," and that the specification "acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." Vitronics, 90 F.3d at 1582; Irdeto Access, Inc. v. Echostar Satellite Corp., 383 F.3d 1295, 1300 (Fed. Cir. 2004) ("Even when guidance is not provided in explicit definitional format, the specification may define claim terms by implication such that the meaning may be found in or ascertained by a reading of the patent documents.") (citations omitted); Novartis Pharms. Corp. v. Abbott Labs., 375 F.3d 1328, 1334-35 (Fed. Cir. 2004) (same); Bell Atl. Network Servs., Inc. v. Covad Communications Group, Inc., 262 F.3d 1258, 1268 (Fed. Cir. 2001) ("[A] claim term may be clearly redefined without an explicit statement of redefinition.").

Phillips v. AWH. Corp., 415 F.3d 1303 (Fed. Cir. 2005) (en banc). Applicants respectfully submit that the Examiner improperly failed to use the specification as a guide to the meaning of the term "pattern." The instant specification makes it clear that, within the context of the present invention, a "pattern" is a regular arrangement of nucleotides. Claim 11 has been amended to make explicit that a pattern is not any random assortment of modified nucleotides:

> wherein said first stretch and/or said second stretch comprises a plurality of groups of modified nucleotides, wherein each nucleotide in each of said groups is modified at the 2'-position and wherein said groups are arranged in a repeating pattern ,

(Emphasis supplied .) Figure 2, and the accompanying description on pages 9 and 10 of the instant application, make clear that a pattern is a regular arrangement. In Figure 2, the two or more nucleotides that each have a modification at the 2'-position are represented by open boxes, and the flanking nucleotide(s) are represented by horizontal dashes. Figures 2A-2C show various alignments of the boxes between the first and second strands. In Figure 2A, the boxes on the first strand are 100% aligned with the boxes on the second strand. In contrast, in Figure 2B the boxes on the first strand are not aligned at all with the boxes on the second strand, and in Figure 2C the boxes on the first strand are only partially aligned at all with the boxes on the second strand. Here, the term "alignment" is used to indicate the arrangement of the patterns of groups as described above, and is not based on the complementarity of the sequences, as asserted by the Examiner. (See Office Action at page 5.). Applicants now address the references in the order set forth in the Office Action.

Agrawal

Claims 11-19, 25-27, 39 and 31-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal. The Examiner states:

> Agrawal discloses a double stranded structure having a self-complementary region wherein one or more ribonucleotides are modified at the 2'-position with a methoxy...[and] the ribonucleic acid disclosed by Agrawal et al. comprises a double stranded structure wherein **only one ribonucleotide** is modified at the 2'-position, therefore the modified ribonucleotide is flanked by unmodified ribonucleotides forming a pattern wherein the self-complementary regions align.

Office Action at page 5; (emphasis supplied). Applicants respectfully traverse. The "pattern" allegedly disclosed by Agrawal is a single modified ribonucleotide flanked on both sides by unmodified ribonucleotides. In contrast, as discussed above, amended claim 11 recites a pattern that represents a plurality (*i.e.*, two or more) of groups of nucleotides that each have a modification at the 2'-position, and one or more flanking groups of nucleotides that flank each group of modified nucleotides. Agrawal does not teach a polynucleotide containing a repeating pattern of a plurality of modified groups and flanking groups and therefore does not teach each and every limitation of the claims. Accordingly, withdrawal of the rejection is requested.

Crooke

Claims 11-16 and 21-23 are rejected under 35 U.S.C. 102(b) as anticipated by Crooke. Specifically, the Examiner states:

> Crooke et al. further discloses a double stranded structure comprising "a pattern of a plurality of groups of modified nucleotides" modified at the 2'-position with a methoxy and flanked by unmodified nucleotides that consist of one to ten nucleotides and wherein the two strands align. (See Office Action at page 6.)

Applicants respectfully traverse. Crooke provides a double-stranded nucleic acid that was used as an RNAse H substrate in which:

> [t]he "sense" strand was an oligoribonucleotide having phosphodiester linkages in an eight-base gap with flanks having either (a) residues with phosphorothioate linkages or (b) 2'-methoxynucleosides with phosphorothioate linkages. The "antisense" strand in both substrates contained 2'-methoxy phosphorothioate wings on either side of an eight-base ribonucleotide gap having either phosphodiester or phosphorothioate linkages (Table 1). (Crooke at col. 50, lines 51-60.)

The molecule disclosed by Crooke therefore contains a single sequence of 8 unmodified ribonucleotides flanked on one or both sides by ribonucleotides that may contain 2'-methoxy phosphorothioate modifications. There is no discernible "pattern" to Crooke's molecule, let alone a repeating pattern of the type recited in the instant claims – it merely has two regions of 2'-modified nucleotides separated by non-modified nucleotides. Accordingly, Crooke does not teach a polynucleotide containing a repeating pattern of a plurality of modified groups and flanking groups and therefore does not teach each and every limitation of the claims. Accordingly, withdrawal of the rejection is requested..

Tuschl

Claims 11-20, 29 and 31-33 are rejected under 35 U.S.C. 102(e) as anticipated by Tuschl et al. (WO 02/44321) ("Tuschl"). The Examiner states:

> Tuschl et al. further discloses a double stranded structure comprising "a pattern of a plurality of groups of modified nucleotides," namely two or four nucleotides modified at the 2'-position with a methoxy, wherein the group is flanked by unmodified nucleotides that consist of one to ten nucleotides (see Figure 14) and further the pattern of two or four nucleotides modified at the 2'-position on the

> first strand is the same as the pattern on the second strand wherein the two strands align. (See Office Action at page 8.)

Thus, the Examiner concludes that Tuschl anticipates claims 11-20, 29 and 31-33. Applicants disagree. Tuschl teaches siRNA duplexes in which:

> [t]he 2'-hydroxyl groups (OH) in the strands of siRNA duplexes were replaced by 2'-deoxy (d) or 2'-O-methyl (Me). 2-nt and 4-nt 2'-deoxy substitutions **at the 3'-ends** are indicated as 2-nt d and 4-nt d, respectively. Uridine residues were replaced by 2'-deoxy thymidine.

Tuschl at page 20, line 28 to page 21, line 2. (Emphasis supplied). Thus, the "pattern" allegedly disclosed by Tuschl is a single group of 2'-modified nucleotides at the 3'-end of each strand bounded by a collection of unmodified ribonucleotides and 2'-deoxy thymidines in place of uridines. In contrast, claim 11 recites a repeating pattern of groups of 2'-modified nucleotides flanked by either unmodified nucleotides or nucleotides with a different modification than the 2'-modified polynucleotides. Accordingly, Tuschl does not teach a polynucleotide containing a repeating pattern of a plurality of modified groups and flanking groups and therefore does not teach each and every limitation of the claims. Accordingly, withdrawal of the rejection is requested.

McSwiggen

Claims 11-19, 21-23, 25-27, 29 and 31-33 are rejected under 35 U.S.C. 102(e) as anticipated by McSwiggen. Specifically, the Examiner states:

> McSwiggen et al. further discloses the double stranded structure comprises "a pattern of a plurality of groups" of 2'-modified nucleotides, flanked by modified or unmodified nucleotides that consist of one to ten nucleotides and the modification at the 2' position can comprise a methoxy or a fluoro wherein the two strands are aligned (see Figure 5).

Office Action at page 10. Applicants respectfully traverse.

McSwiggen describes chemically modified siRNA constructs in which "all pyrimidine nucleotides that may be present are 2'-O-methyl modified nucleotides." (McSwiggen at paragraphs [0146]-[0147].) The positioning of pyrimidine nucleotides in any given sequence is determined by the target sequence of the siRNA and it therefore follows that the "pattern" of 2'-

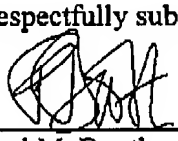
modified nucleotides is similarly determined. Accordingly, McSwiggen fails to disclose any "pattern" of modified nucleotides at all – no person of ordinary skill would be able to discern anything resembling a pattern of 2' modified nucleotides in McSwiggens siRNA molecules, let alone a repeating pattern of the type recited in the instant claims. Accordingly, McSwiggen does not teach a polynucleotide containing a repeating pattern of a plurality of modified groups and flanking groups and therefore does not teach each and every limitation of the claims. Accordingly, withdrawal of the rejection is requested.

CONCLUSION

In view of the foregoing amendments and remarks, applicants respectfully submit that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-3840. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).**

Respectfully submitted,



Date: July 12, 2006

Paul M. Booth
Attorney for Applicant
Reg. No.: 40,244

Proskauer Rose LLP
1001 Pennsylvania Avenue, NW
Suite 400
Washington, DC 20004
Telephone: 202.416.6800
Facsimile: 202.416.6899
CUSTOMER NO: 61263

Customer No. 61263